Quantitative Intravital Microscopy of Liver Transport

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Because if its unique ability to collect fluorescence images from deep in biological tissues, intravital multiphoton microscopy has become a valuable tool in several areas of biological research, including neurobiology, cancer biology and immunology. Here we describe methods of quantitative intravital microscopy that we have developed to characterize cholestatic liver injury. Special methods of tissue immobilization, multiphoton microscopy and digital image analysis were developed to support dynamic measurements of the kinetics of transport from the sinusoids into the cytosol and from the cytosol into the bile canaliculi in individual hepatocytes in vivo. Using a combination of different fluorescent probes, we have combined transport assays with measures of microvascular function, inflammation and cell viability to provide integrated measures of liver injury. The sensitivity of this approach is demonstrated in quantitative analyses of the acute effects of cholestatic drugs and the effects of chronic kidney disease.